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Toxicity of Filtrates of Staphylococcus Aureus From Human Infections and From Normal Nasopharynx.

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In 1899 Von Lingelscheim[1] observed necrosis in the skin of rabbits following the intracutaneous injection of staphylococcus filtrates. Neisser and Wechsberk[2] repeated the original experiments of Lingelscheim and studied the toxic properties of the filtrates more fully. They demonstrated both active and passive immunity in rabbits and found the toxic qualities of the filtrate to be extremely thermolabile. The filtrates no longer gave cutaneous reactions after heating at 56° C. More recently Parker[3] and her associates have carried out experimental work along the same line. They find that filtrates of staphylococcus grown under proper conditions cause necrosis in the skin of rabbits. They obtain antitoxic serum in rabbits and horses. This antitoxin prevents the necrosis in the rabbit, and neutralizes staphylococcus filtrate, according to the law of multiples. In their first experiments few of the strains with which they were working gave toxic filtrates. Later filtrates from 13 or 14 strains gave cutaneous reactions neutralized by a common antitoxic serum.

When filtrates of bacteria give cutaneous reactions of this type there is a possibility that the toxicity of the filtrates may be associated with the virulence of various strains. We have studied 31 strains of *Staphylococcus aureus* with this possibility in view. The strains selected were all hemolytic. They were obtained from two sources. First, from infectious processes including furuncles, abscesses, acute staphylococcus anginas and from the blood stream in cases of septicaemia, and second from the nasopharynx of normal individuals who were carriers of staphylococcus. The first subculture of each strain was grown in 4 per cent proteose peptone broth for 4 days in an atmosphere of carbon dioxide. Parker[3] has found this method especially suitable for the production of toxin. The sterile filtrates were then tested in the skin of rabbits to determine the minimum reacting dose, control experiments were carried out with filtrates boiled for 10 minutes, and neutralization tests made with antitoxic horse and rabbit sera. The horse serum was prepared by Parker.

TABLE I.

Comparison of the toxicity of Staphylococcus aureus filtrates and neutralization reactions with antitoxic sera.

Source	Cutaneous reactions in rabbits					Boiled filtrate	Normal rabbit serum	Rabbit antitoxin	Horse antitoxin
	1 cc.	.1 cc.	.05 cc.	.01 cc.	.005 cc.				
Abscess	+	+	+	+	—	—	+	—	—
Furuncle	+	+	+	+	—	—	++	—	—
Furuncle	+	+	—	—	*	—	++	—	—
Furuncle	+	+	+	—	*	—	++	*	—
Furuncle	+	+	+	—	*	—	*	*	—
Furuncle	+	+	+	—	*	—	++	—	—
Furuncle	+	+	+	—	*	—	++	—	*
Furuncle	+	+	—	—	*	—	++	*	—
Furuncle	+	+	+	—	*	—	+	-	—
Furuncle	+	+	+	+	±	—	++	—	—
Bloodstream	+	+	+	—	*	—	++	*	—
Furuncle	+	+	+	—	*	—	++	*	—
Abscess	+	+	+	+	—	—	++	*	—
Angina	+	+	+	++	±	—	+	—	—
Furuncle	+	+	+	±	—	—	++	-	*
Bloodstream	*	+	+	±	-	—	*	—	—
Pharynx	+	+	+	+	—	—	+	—	—
Pharynx	+	+	+	±	—	—	*	*	—
Pharynx	+	+	+	++	+	—	+	—	—
Pharynx	+	+	+	++	±	—	++	—	—
Pharynx	+	+	+	++	—	—	++	—	—
Pharynx	+	+	+	++	+	—	*	*	—
Nose	—	—	—	*	*	*	*	*	*
Nose	+	+	+	—	*	—	*	*	—
Nose	—	—	*	*	*	*	*	*	*
Nose	+	+	—	—	*	—	+	—	—
Nose	+	+	+	—	*	—	*	*	—
Nose	+	+	+	—	*	—	+	—	—
Nose	—	—	*	*	*	—	*	*	*
Pharynx	+	+	—	—	*	—	*	*	—
Pharynx	*	+	+	+	+	—	*	*	—

* Reaction not done.

The data have been arranged in the accompanying table. The strains have been placed in two groups. The first includes strains from the infections and the second those from normal carriers. After each strain the reaction obtained in rabbits with decreasing amounts of filtrate has been indicated in the appropriate column. The doses employed were 1 cc., 0.1 cc., 0.05 cc., 0.01 cc., and 0.005 cc. of filtrate, The results of neutralization with antitoxic sera, normal rabbit serum, and of thermolability have been indicated in additional columns.

An analysis of this table shows that the toxins produced by the various strains of *Staphylococcus aureus* which we have studied are apparently identical, since the reaction obtained with each filtrate could be prevented with the same antitoxic sera in all instances, and the toxic properties of all the filtrates had the same degree of thermolability. This applies to strains from both groups studied. Among the strains obtained from the acute infections there appears to be no relationship between the severity of the infection clinically, and the ability of the corresponding strain to produce toxin. When the two groups are compared in regard to toxin production there is no significant difference. The only noteworthy feature is the fact that all the strains from infections produced toxin, while three of the strains from the nasopharynx either produced none, or produced such small amounts that no reaction followed the intracutaneous injection of filtrate.

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[1] Von Lingelscheim, W., *Beitr. z. Exp. Ther.*, 1899, i, 49.

[2] Neisser, M., Kolle and Wasserman, *Handbuch der Pathogenen Mikroorganismen*, Jena, 2nd Edition, 1912, iv, 375.

[3] Parker, J. T., *J. Exp. Med.*, 1924, xl, 761; Parker, J. T., Hopkins, J. G., and Gunther, A., PROC. SOC. EXP. BIOL. AND MED., 1926, xxiii, 344; Parker, J. T., and Banzhof, E. J., *J. Immunol.*, 1926, xiii, 25.